CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-366

ADMINISTRATIVE DOCUMENTS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: **75-366** Dates of Submission: **April 13 and May 22, 1998**

Applicant's Name: **Eon Labs Manufacturing, Inc.**

Established Name: **Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg**

Labeling Deficiencies:

1. CONTAINER 80 mg (100s) 120 mg, 160 mg, 240 mg (100s and 500s)

   a. Correct the hyphenation of the word "temperature".

   b. Increase the blank vertical space between the left panel and the main panel.

   c. The statement "Dispense contents..." appears to run into the text on the main panel.

   d. 160 mg - 500s only - Delete the hyphen in the word "accompanying".

2. INSERT

   a. GENERAL COMMENTS

      i. There is no need to capitalize "sotalol" unless required by sentence structure.

      ii. Be consistent with the prominence of the subsection headings throughout the text.

      iii. Replace the hyphen with the word "to" when expressing a range throughout the text.

   b. DESCRIPTION

      i. Delete the word "tablets" in the first sentence.

ii. "anhydrous lactose" rather than "lactose anhydrous".

iii. "pregelatinized" (spelling).

c. CLINICAL PHARMACOLOGY

i. Delete "hydrochloride" and "hydrochloride tablets" throughout this section wherever it occurs except in the following places:

A). Mechanism of Action - second sentence

B). Hemodynamics - first sentence

C). Clinical Actions

1). Second occurrence in the paragraph beginning "In a double-blind..."

2). First occurrence in the paragraph beginning "In a large double-blind ..."

D). Pharmacokinetics - second occurrence

ii. Delete "tablets" in the first sentence of the "Hemodynamics" subsection.

d. INDICATIONS AND USAGE

i. Revise the section title as seen above.

ii. Delete "hydrochloride" and "hydrochloride tablets" throughout this section wherever it occurs except in the first sentence.

e. CONTRAINDICATIONS

Sotalol hydrochloride is contraindicated ...

f. WARNINGS

i. Delete "hydrochloride" throughout this section wherever it occurs except in the following places:

A). Second occurrence in the paragraph beginning "The applicability of ..."

B). Abrupt withdrawal - the second occurrence

ii. Recent Acute MI, second sentence - "from" (spelling)

iii. Non-Allergic Bronchospasm - Increase the spacing between the bolded capitalized words.

g. PRECAUTIONS

i. Delete "hydrochloride" throughout this section.

ii. Decrease the prominence of the subsection title "**DRUG INTERACTIONS**".

iii. "**Pregnancy**: Pregnancy Category B:" should be the subsection title.

iv. Pediatric Use - "pediatric patients" rather than "children".

h. ADVERSE REACTIONS

i. Delete "hydrochloride" throughout this section.

ii. Table - "proarrhythmia" (lower case "p")

iii. Potential Adverse Effects, first paragraph, last sentence

A). "photosensitivity" (delete the hyphen)

B). "pruritus" (spelling)

i. OVERDOSAGE

Symptoms and Treatment of Overdosage

i. First sentence - "hypoglycemia" (delete hyphen)

ii. Fourth sentence - "concentrations" (plural)

iii. Delete the second occurrence of "*Bradycardia or Cardiac Asystole*".

j. DOSAGE AND ADMINISTRATION

i. Delete "hydrochloride" in the second sentence and in the sentence immediately before the "**Dosage in Renal Impairment**" subsection and all others which occur from this subsection through to the "HOW SUPPLIED" section.

ii. Dosage in Renal Impairment

A). Decrease the prominence of the heading.

B). Delete the last paragraph of this subsection and replace it with the following text:

... table above).

Pharmacokinetic findings in patients requiring chronic hemodialysis is limited to six patients in two studies. In these patients, terminal elimination half life is prolonged to 40 hours in the interdialysis period and approaches 7 hours during dialysis. It is estimated that 20% to 40% of sotalol is removed during dialysis and that a slight rebound of plasma concentration is noted post dialysis. Extreme caution must be taken in renal failure requiring hemodialysis, usual parameters of safety and efficacy (heart rate, QT interval and control of arrhythmia) must be closely monitored.

k. HOW SUPPLIED

i. "tablets" (lower case "t")

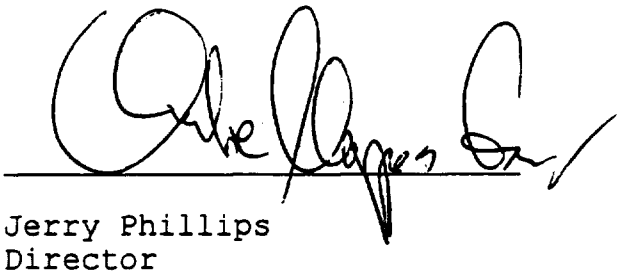
ii. We encourage the use of the NDC number in this section.

iii. Insert a blank space between the word "closure" and "(as required)".

iv. We encourage you to relocate the symbol "**Rx only**" to under the Title of the insert.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval or 12 final printed copies for a full approval of this application. If draft labeling is provided, please be advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. In addition, you should be aware that color and other factors (print size, prominence, etc.) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval. Please revise your container labels and insert labeling, as instructed above, and submit in final print.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.



Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Food and Drug Administration
Rockville MD 20857

ate: *April 29, 1999*

o: Food and Drug Administration Pre-approval Laboratory
Philadelphia District Laboratory, HFR-MA160
US Customhouse
2nd and Chestnut Streets, Room 900
Philadelphia, PA 19106
Attention: Wayne Smith

~~215-597-4390~~ 215-597-4390 x4609

rom: Maria C. Shih, Review Chemist, HFD-643 M.C. 4/30/99

hrough: Richard Adams, Chemistry Team Leader, HFD-643 R. C. Adams 5/3/99

bject: Laboratory Assignments for ANDA Methods Validation (MV)

NDA No: 75-366 **Product:** Sotalol HCl tablets, 80 mg (lowest dosage)

pplicant: Eon Labs

firm has submitted their regulatory methods for this drug product. These proposed atory analytical methods should be validated by your laboratory as this subject drug product not have a USP monograph.

structed under the PRE-APPROVAL INSPECTION/INVESTIGATIONS program (CP 832), you are requested to obtain samples of the subject drug product including impurity rence standards (if any) from the applicant at the address given below:

Eon Labs
Attention: Sadie M. Ciganek
227-15. Conduit Avenue
Laurelton, NY 11413

Telephone: 718-276-8600 ext. 330
FAX: 718-949-3120

completion of methods validation, please send work sheets, all attachments, conclusions, commendations directly to the review chemist at the address given below:

Maria C. Shih
Office of Generic Drug
7500 Standish Place
Rockville, MD 20855

Telephone: (310) 827-5849
FAX: (301) 443-3839

d is one methods validation (MV) package with MV request forms (2871 & 2871a).